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Structure of the human gene for lysosomal di-N-acetylchitobiase.

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Chitobiase is a lysosomal glycosidase that acts during the ordered degradation of asparagine-linked glycoproteins to cleave the core chitobiose unit at its reducing end. Human chitobiase is expressed in significant amounts, while bovine chitobiase is produced at extremely low levels. To begin to understand this species-dependent expression, we determined the gene structure of human chitobiase. The human chitobiase gene (CTB S) is approximately 20 kb comprising seven exons varying from 0.1 to 2.3 kb and six introns of 0.3 to 8 kb. The previously characterized partial bovine chitobiase gene structure is similarly organized including exon and intron sizes and locations, but the human and bovine 5'-flanking regions differ significantly. 5'-RACE analysis of human chitobiase cDNA revealed only one transcriptional start site 45 bp upstream of the ATG translation initiation site. Computer analysis of the human chitobiase gene 5'-flanking region shows characteristics of a typical housekeeping gene. The putative promoter region contains a distal TATA box, and there are several Sp-1 and AP-2 cis elements. In contrast, bovine chitobiase gene 5'-flanking region shows totally different structures and may contain several silencers. A partial art-2 segment which is an artiodactyl Alu-like repetitive sequence, is also present. These evolutionary differences in the 5'-flanking region of the chitobiase genes from human and bovine could account for the widely varied expression levels of the hydrolase within these two species.

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